98. (New) A vaccine for protecting animals against at least one biological activity of wild-type SPE-A comprising: an effective amount of at least one mutant SPE-A toxin according to claim 91.

99. (New) A pharmaceutical composition comprising: a mutant SPE-A according to claim 91 in admixture with a physiologically acceptable carrier.

100. (New) A method for protecting an animal against at least one biological activity of a wild type SPE-A comprising: administering a vaccine according to claim 97 to an animal.

101. (New) A method for reducing symptoms associated with toxic shock comprising: administering a vaccine according to claim 97 to an animal.

REMARKS

Applicants have received and reviewed the final Office Action dated October 3, 2000. By way of response, Applicants have cancelled claims 1, 3-9, 12-14 and 17-29 and present new claims 30-101. Claims 30-101 are pending. No new matter is introduced. Applicants submit that the newly presented claims are supported by the specification.

For the reasons given below, Applicants respectfully submit the amended and newly presented claims are in condition for allowance, and notification to that effect is earnestly solicited.

Petition for Extension of Time

It is noted that a two-month petition for extension of time is necessary to provide for timeliness of the response. A request for such an extension is made extending the time for response from January 3, 2001 to March 3, 2001.

The Examiner Interview

Applicants and Applicants undersigned representative thank the Examiner for courtesies extended during the telephone interview of January 11, 2000. During the interview, the Examiner and Applicants' undersigned representative discussed the status of the application noting that a rejection under section 112 second paragraph remained, that several rejections had been withdrawn, and that the provisional obviousness-type double patenting rejection remained provisional. Applicants' undersigned representative expressed appreciation that the Examiner had withdrawn several rejections in light of the previous amendment and remarks. Applicants' undersigned representative expressed hope that he and the Examiner could work together to arrive at allowable claims for the present application.

The discussion of the outstanding section 112 second paragraph rejection began with consideration of use of the term "substantially". While maintaining the rejection, the Examiner expressed willingness to listen to reasoning supporting use of the term "substantially". First, Applicants' undersigned representative noted that the phrase "substantially corresponding to" objected to by the Examiner was an unnecessary limitation that could be readily eliminated from the claims. With regard to the other occurrences of the term, Applicants' undersigned representative pointed out that the MPEP expressly approves of the use "substantially" at 2173.05(b) under subheading D and reiterated that the term was defined in the specification. The Examiner consulted with other examiners on this point and stuck by her objection to the term substantially. Applicants appreciate the promptness and courtesy with which the Examiner undertook these consultations and telephoned Applicants' undersigned representative to discuss them.

The discussion then turned to the Examiner's objection to claims reciting residues of a protein without reciting the entire protein sequence. Applicants' undersigned representative noted that patents, patent attorneys, and scientists routinely referred to proteins by name to indicate a protein of a particular amino acid sequence. The name SPE-A refers to a protein that is well-known and has little sequence variation in nature. The Examiner considered this reasoning, discussed this point with a more experienced patent examiner, and indicated her willingness to allow claims that identified SPE-A by name. Again, Applicants appreciate the

promptness and courtesy with which the Examiner undertook these consultations and telephoned Applicants' undersigned representative to discuss them.

In the present amendment, Applicants present claims that the Examiner indicated should be allowable. As discussed below, Applicants have removed the term "substantially" from the claims. The claims identify SPE-A by name. Applicants thank the Examiner for the thoughtfulness that she exhibited during the interview, the effort she expended in consulting with other examiners, and the courtesies extended throughout the interview.

Guide to the Newly Presented Claims

The newly presented claims generally correspond to the previous claims that the Examiner indicated were allowable. The independent claims have been slightly modified to clarify reference to residues recited in the previous independent claims. Many of the dependent claims include limitations identical to those employed in the previous dependent claims.

Newly presented independent claims 30 and 50 generally correspond to previous independent claim 1, and newly presented independent claims 77 and 91 generally correspond to previous independent claim 19. Previous independent claim 1 referred to "an amino acid substitution in ... or a combination of such substitutions ", newly presented independent claims 30 recites "a combination of amino acid substitutions in". Previous independent claim 1 referred to substitution in an helix, a strand, at a cysteine, or a combination of such substitutions, newly presented independent claim 50 refers to "a substitution in a domain B beta strand comprising residues 41 through 47 of SPE-A". Previous independent claim 19 recited "amino acid substitution at ...or a combination thereof", newly presented independent claim 77 recites "a combination of amino acid substitutions at". Previous independent claim 19 recited five residues that can be a site of substitution, newly presented claim 91 recites three of these residues.

Newly presented the dependent claims 31-37 generally correspond to previous dependent claims 3-9. Newly presented dependent claim 38 further limits independent claim 30. Newly presented dependent claims 39-49 generally correspond to previous dependent claims 4-9, 12-14, and 17-18. Newly presented dependent claim 51 further limits independent claim 50. Newly presented dependent claims 52-55 generally correspond to previous dependent claims 5-8.

Newly presented dependent claims 56 and 57 further limit independent claim 50. Newly presented dependent claims 58-62 generally correspond to previous dependent claims 4-8. Newly presented dependent claims 63 and 64 further limit claim 50. Newly presented dependent claims 65-76 generally correspond to previous dependent claims 4-9, 12-14, and 17-18.

Newly presented dependent claims 78-82 generally correspond to previous dependent claims 20-24. Newly presented dependent claim 83 further limits independent claim 77. Newly presented dependent claims 84 and 85 generally correspond to previous dependent claim 20. Newly presented dependent claims 86-90 generally correspond to previous dependent claims 25-29. Newly presented dependent claims 92, 94, and 96 generally correspond to previous dependent claim 20. Newly presented dependent claims 93 and 95 further limit claims 92 and 94, respectively. Newly presented dependent claims 97-101 generally correspond to previous dependent claims 25-29.

Rejection of Claims Under § 112, Second Paragraph

The Examiner rejected claims 1, 3-9, 12-14 and 17-29 under 35 U.S.C. § 112, second paragraph. Although this rejection has not been raised for the newly presented claims, it is addressed insofar as it might apply. The Examiner objected to certain terms and phrases employed in the claims. Applicants respectfully traverse this rejection.

In particular, the Examiner objected to the use of the phrases "mutant SPE-A toxin" or "wild type SPE-A toxin" together with positions of substituted amino acids. As described herein above in the discussion of the Examiner Interview, the name SPE-A refers to a protein that is well-known and has little sequence variation in nature. Although many alleles of the gene encoding this protein exist, the vast majority of these alleles encode the same SPE-A protein sequence and a few encode variants, typically variants that differ by only a single amino acid substitution. This is described in Exhibit A, Nelson et al. J. Exp. Med. 174(5):1271-1274 (1991), which Applicants invite the Examiner to read and evaluate. Thus, the name SPE-A and reference to amino acid locations in that protein unambiguously identify the protein and location of residues.

Further, the SPE-A sequence can be found in Figure 3 as well as the sequence listing. The amino acid number designations are made by reference to this sequence. The name SPE-A and reference to amino acid locations in that protein unambiguously identify the protein and location of residues.

The Examiner objected to the recitation of phrases including the term "substantially", which can be found in claims 1, 12 and 25. Solely to advance prosecution of the present application and not to acquiesce to the rejection, Applicants have removed the term "substantially" from claims 1, 12, and 25. This renders this portion of the rejection moot.

Applicants reiterate their belief that the term substantially was used in an acceptable manner in the claims. The MPEP expressly approves of the use "substantially" at 2173.05(b) under subheading D, citing uses of this term similar to its uses in the claims of the present application. Applicants also reiterate that the phrases employing the term substantially are defined in the specification, as was discussed in the previous Amendment and Response.

Applicants submit that these definitions remain valid for the same phrases lacking the term substantially. That is "nonlethal" refers to a claimed mutant SPE-A toxins that substantially nonlethal in rabbits when administered by miniosomotic pump (as described in Example 2) at the same or greater dose than a wild type SPE-A toxin. Specifically, the mutant SPE-A is nonlethal if when administered to a rabbit at the same dose as the wild type toxin, less than about 10-20% of rabbits die. Lack of enhancement of endotoxin shock can be evaluated in rabbits as described in Example 4. Lack of enhancement of endotoxin shock is seen when less than about 25% of the animals develop shock when the mutant SPE-A toxin is co-administered with endotoxin as compared to wild type SPE-A activity at the same dose. The phrases employing the term substantially are defined in the specification, this term was used appropriately, and the phrases lacking this term are also appropriate and well defined.

Accordingly, it is believed that the amended and newly presented claims fully comply with § 112, second paragraph, withdrawal of this rejection is respectfully requested.

Provisional Double Patenting Rejection of Claims

The Examiner rejected claims 1-14, and 17-18 under statutory type and/or obviousness-type double patenting as being unpatentable over the copending Application No. 08/973,391. Although this rejection has not been raised for the newly presented claims, it is addressed insofar as it might apply. Applicants note that at this time this rejection remains provisional. Claims in copending Application No. 08/973,391 have not yet been allowed. Therefore, Applicants believe that withdrawal of this provisional rejection is appropriate.

Summary

In summary, each of claims 30-101 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below, if the Examiner believes that doing so will expedite prosecution of this patent application.

Respectfully submitted,

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Date: March 2, 2001

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Exhibit A

Nelson et al. J. Exp. Med. 174(5):1271-1274 (1991)

Accompanying the AMENDMENT & RESPONSE for application serial no. 09/308,830